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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,516	04/03/2002	Michel G. Bergeron	GGD-31611-PCTUS	5405

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,516	BERGERON ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/2/01; 4/3/02;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-23 are pending.

2. Applicant's Status Inquiry, filed 10/23/03 and 2/20/04 is acknowledged. This Office Action should serve in response to said inquiry

3. Applicant's election of Group I, claims 1-20 drawn to a formulation for targeting an infectious agent which requires a HLA-DR host membrane during its life cycle or a HLA-DR expressing host cell or both comprising a ligand capable of binding to said host membrane protein, said ligand being coupled to a lipid comprising vesicle, filed 6/22/04, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 21-23 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

5. Claims 1-20, drawn to a formulation for targeting an infectious agent which requires a HLA-DR host membrane during its life cycle or a HLA-DR expressing host cell or both comprising a ligand capable of binding to said host membrane protein, said ligand being coupled to a lipid comprising vesicle, are being acted upon in this Office Action.

6. Claims 2-20 are objected to because "A" should have "The" for said dependent claims.

7. Claim 19 is objected to because "ddl" should have been "ddI".

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of all formulation for targeting *all* infectious agent which acquires *any* HLA-DR host membrane protein during its life cycle or *any* HLA-DR expressing host cell or both, said formulation comprising *all* ligand capable of binding to *all* host membrane protein (claim 1), *all* ligand binding to any host membrane such as the ones recited in (claim 10), all antibody and fragment thereof (claim 11) coupled to all lipid-comprising vesicle or liposome (claims 1-2) or the specific liposome (claims 3-9), and all drug effective against all disease caused by any infectious agent (claim 12).

The specification discloses only a formulation for targeting HIV which acquires a HLA-DR class I host membrane protein during its life cycle and HLA-DR class I expressing host cell said formulation comprising an antibody or binding fragment that binds to HLA-DR class I on host membrane protein wherein the antibody or binding fragment is being coupled to a liposome comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging between 10:1 and 1:1, wherein the acyl chains are either saturated or unsaturated and have between 14 and 18 carbon atoms in length.

With the exception of the specific formulation mentioned above, there is insufficient written description about the structure associated with function of *all* ligand and all antibody capable of binding to host membrane expressing which HLA-DR wherein the ligand being coupled to all lipid-comprising vesicle or liposome for the claimed formulation. Further, there is inadequate written description about which "infectious agent" other the HIV requires HLA-DR host membrane during its life cycle and/or HLA-DR expressing host cell that the claimed formulation targets.

Given the lack of a written description of *any* additional representative species of formulation comprising any ligand capable of binding to host membrane, or any antibody and fragment thereof that bind to all host membrane being coupled to any lipid-comprising vesicle for targeting all infectious agent which requires a HLA-DR host membrane protein during its life cycle, or a HLA-DR expressing host cell or both, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to describe the genus for the claimed formulation. Thus, Applicant was not in possession of the

claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Markush group recited in dependent claim 10 includes histocompatibility protein class I and II (genus), which is improper because "HLA-DR" in claim 1 is a class I major histocompatibility complex protein (specie).

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-2, 10, 11, 13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Phillips *et al* (J Immunol 152(6): 3168-74, March 1994; PTO 1449).

Phillips *et al* teach a formulation for targeting a HLA-DR expressing host cell such as T cell comprising a ligand such as whole monoclonal rat anti-mouse CD4 antibody or F(ab)2 fragment thereof that is capable of binding to host membrane protein such as CD4 wherein the reference ligand is coupled to a lipid-comprising vesicle or immunoliposome such as dipalmitoylphosphatidylcholine, in a mixture with diacylphosphatidylglycerol in a 10: 1 (See abstract, page 3169, Materials and Methods, in particular). The reference CD4+ T cell is a lymphoid cell and inherently expresses the HLA-DR, CD54, CD3, IL-2 receptor, transferring receptor and cytoskeletal proteins. Thus, the reference teachings anticipate the claimed invention.

14. Claims 1-2, 10-11, 13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/10585 (April 11, 1996; PTO 1449).

The WO96/10585 publication teaches a formulation comprising various ligand such as whole antibody such as anti-CD4, anti-CD8, anti-ICAM-1 that is capable of binding to host membrane protein such as CD4, CD8, ICAM-1 (CD54), respectively, and the reference ligands are coupled to a lipid-comprising vesicle or liposome (See page 15, second paragraph, claim 12 of WO96/10585 publication, in particular). The reference host cell such as CD4+ T and CD8+ cells are lymphoid cell that inherently expresse the HLA-DR, CD3, IL-2 receptor, transferring receptor and cytoskeletal proteins. Thus, the reference teachings anticipate the claimed invention.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1-9, 12, 14, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,773,027 (June 30, 1998; PTO 892) in view of Zelphati *et al* (Antisense Res Dev 3(4): 323-38, 1998; PTO 1449).

The '027 patent teaches a formulation for treatment of viral disease such as HIV which comprises a lipid vesicle or liposome that comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging between 10:1 and 1:1, wherein the acyl chains are either saturated or unsaturated and have between 14 and 18 carbon atoms in length (See claim 1 of '027 patent, col. 3, lines 58-62, in particular). The reference formulation wherein

the lipid component comprises a polyethyleneglycol derivative of diacylphosphatidylethanolamine (see claim 2 of '027 patent, in particular). The reference formulation wherein the liposome comprises a polyethyleneglycol derivative of diacylphosphatidylethanolamine and wherein the polyethyleneglycol has a molecular weight between about 500 and 5000 Daltons (See claim 11 of '027 patent, in particular). The '027 patent also teaches a formulation wherein the liposome comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio of 10:3 (See col. 3, liens 46-47, in particular) and a formulation wherein the lipid component comprises a mixture of diacylphosphatidylcholine:diacylphosphatidylglycerol:diacylphosphatidylethanol-amine-polyethyleneglycol in a molar ratio of 10 to 3 to 1.45 which is between the claimed 0.1-3 (See col. 5, lines 46-47, in particular). The reference formulation further encapsulated a drug such as AZT, ddI, ddC, saquinavir, ganciclovir, foscarnet and ribavirin for treating viral infection (See claims 7, 9-10 of '027 patent, in particular). The '027 patent further teaches that the reference liposome formulation can be modified by coupling of antibody molecules to enhance the targeting of the liposome to the specific cells (See col. 4, lines 11-13, in particular) that are HIV reservoirs as well as marked improvement of the pharmacokinetics of drugs (See abstract, in particular). The '027 patent teaches that targeted delivery of anti-viral agents upon encapsulated in liposome could increase efficacy, reduce toxicity of anti-viral agents in humans suffering from AIDS or other viral diseases, improve drug bioavailability upon encapsulation of drugs into liposome that could reduce the dose of anti-viral agents used in conventional therapy as well as the frequency of administration of anti-HIV agents therefore improving the quality of life of patients with AIDS and other viral diseases (See col. 2, lines 25-31, col. 9, lines 7-12, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the formulation wherein ligand is any antibody that binds to the target cells instead of a ligand capable of binding to host membrane protein that targets an infectious agent which acquires a HLA-DR host membrane protein during its life cycle or a HLA-DR expressing host cell or both.

The invention in claim 20 differs from the teachings of the reference only in that the formulation wherein the protein is HLA-DR and said ligand is an anti-Fab' antibody fragment directed against said host membrane protein.

Zelphati *et al* teach a formulation for targeting an infectious agent such as HIV which acquires a HLA-DR, or CD4 host membrane protein during its life cycle and HLA-DR and CD4

expressing host cell such as T cell line CEM wherein the reference formulation comprises immunoliposome encapsulated drug such as HIV-1 rev and tat gene-specific anti-sense phosphodiester or phosphorothioate oligonucleotides coupled to various ligands such as protein A that binds to the Fc region of antibodies to CD4 (anti-CD4 antibody BL4), anti-human CD7 or anti-HLA antibodies that bind to HLA protein on the reference T cells (See page 328, last paragraph, page 326, first paragraph, in particular). Zelphati *et al* teach liposome containing anti-sense (S-anti-*rev*, n-anti-*rev* and n-anti-*tat*) targeted to HIV infected CEM cells by HLA-specific antibodies (B1.23.2) inhibited HIV-p24 expression in de novo infected cells (See page 329 last paragraph, in particular). Zelphati *et al* teach that CD4 molecules are effectively downmodulated in chronically infected cells but the level of expression of HLA class I molecules on chronically infected cells are unaltered (See page 329, in particular). Zelphati *et al* teach that CD7 and HLA class I molecules expressed on T cells are good targets for specific delivery of liposome-encapsulated methotrexate (See page 329, in particular) and improved efficiency when drug encapsulated immunoliposomes were directed to HLA DR1 molecules expressed by targeted cells (See abstract, page 331, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute any antibody in the formulation as taught by the '027 patent for the ligand such as anti-HLA antibody that targets the drug encapsulated liposome to the infectious agent such as HIV or a HLA-DR expressing T cells (HIV reservoir) or both as taught by Zelphati et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Zelphati *et al* teach that ligand such as HLA class I molecules expressed on T cells are good targets for specific delivery of liposome-encapsulated drug to chronic infected T cells because these molecular are down regulated (See page 329, abstract, page 331, in particular). The '027 patent teaches that targeted delivery of anti-viral agents upon encapsulated in liposome could increase efficacy, reduce toxicity of anti-viral agents in humans suffering from AIDS or other viral diseases, improve drug bioavailability upon encapsulation of drugs into liposome that could reduce the dose of anti-viral agents used in conventional therapy as well as the frequency of administration of anti-HIV agents therefore improving the quality of life of patients with AIDS and other viral diseases (See col. 2, lines 25-31, col. 9, lines 7-12, in particular).

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

20. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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